Submission of
Lot-distribution Data to the
Food and Drug Administration

May 14, 1999

Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Biostatistics and Epidemiology
Rockville, Maryland

301-827-3974

1.0 Introduction:

Historically, manufacturers have submitted data to the FDA in the form of printed reports ("hard-copy"), as required by 21 CFR 600.81. This data is currently manually compiled into the FDA's secure database for use in vaccine safety analysis. In accordance with current automation initiatives, the FDA is currently moving to submission of this data to the FDA in a computer-readable format. Although establishing electronic reporting will initially require additional effort by both the FDA and the submitting manufacturers, the resultant process will increase the accuracy and timeliness of the data.

The FDA has chosen the "ASCII flat-file" format standard to be used for lot distribution data. This document describes the "ASCII flat-file" format for lot distribution data and how to obtain and use an FDA-supplied verification program. The flat-file format described here is derived from "Distribution Data Preferred Format, 21 CFR 600.81".

2.0 Relationships within Data:

Much of the data required for submission by 21 CFR 600.81 is interrelated. The relationships between "label lot", "fill lot", and "bulk lot" numbers require examination in detail. It should be noted first, however, that different types of manufacturers naturally *significantly* different manufacturing processes. As a result, the explanations of "label lot", "fill lot", and "bulk lot" provided below should be used only as a rough guide to the use of these fields. More specifically, the diagrams here are based on the manufacturing processes used by vaccine manufacturers. Other manufacturers, such as blood products should largely discount the diagrams below, and rely on the precise definitions given in section **3.1.1 Data Element Descriptions**, although it is useful to briefly examine figures 1-3 as a starting point.

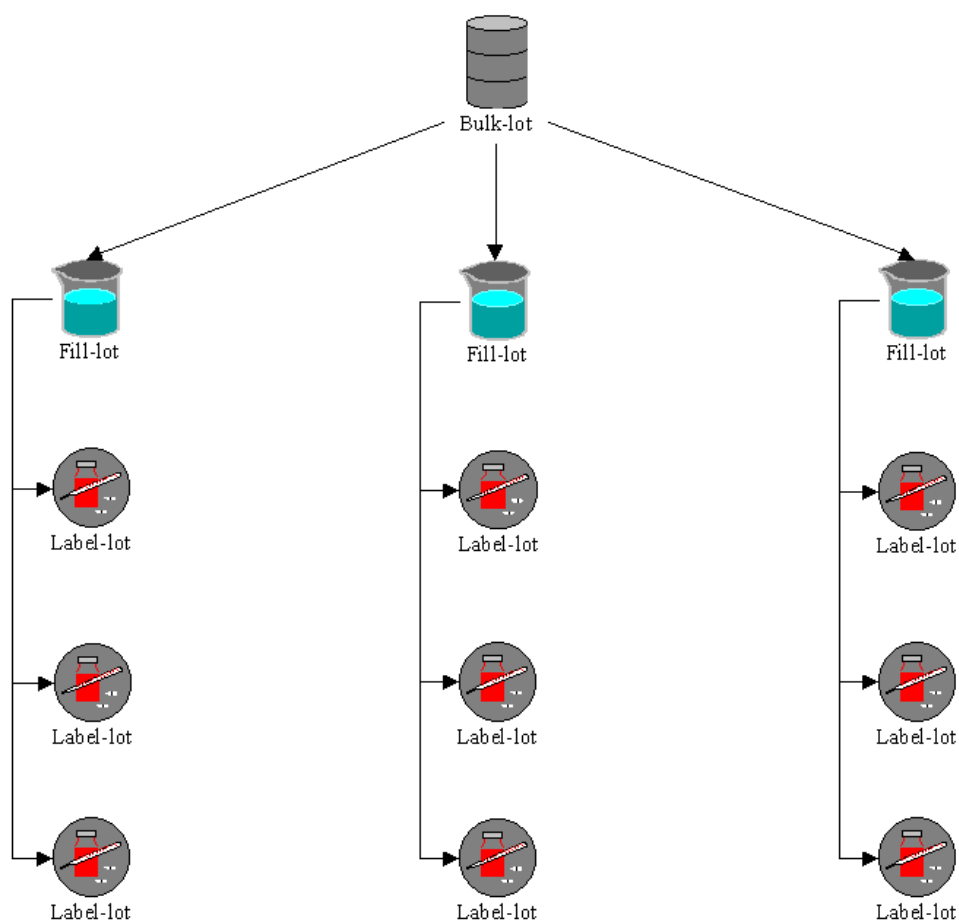The relationships between lot identifiers are illustrated in the following diagrams.

Figure 1

Figure 1 illustrates the most common case for monovalent vaccines, where the largest units of manufacture are divided into successively smaller units until a final label lot is obtained.
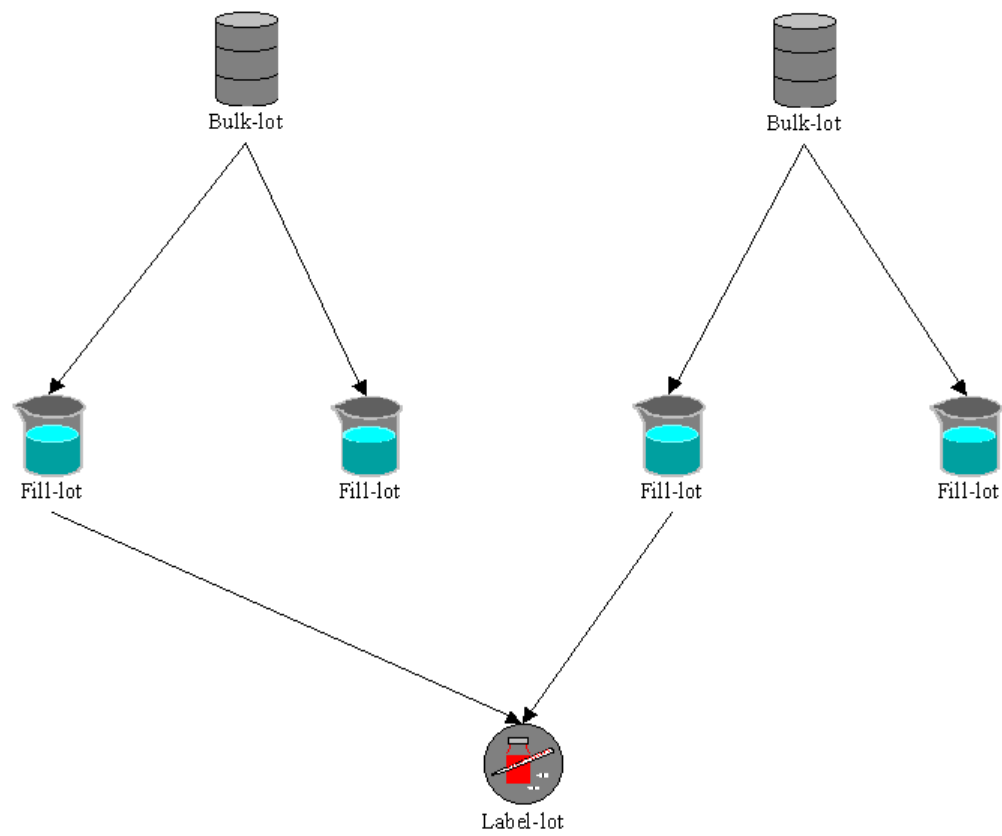
Figure 2

Figure 2 shows the less frequent occurrence of polyvalent vaccines (such as DT).

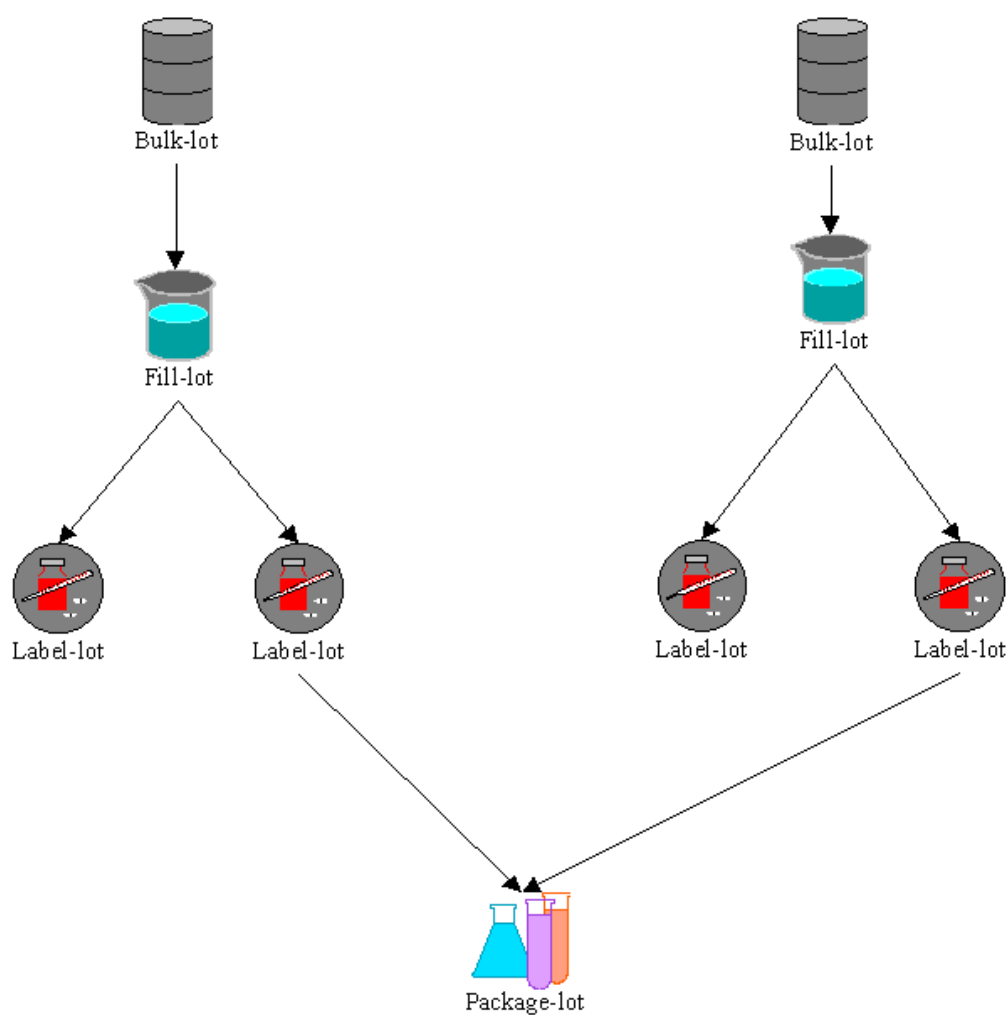## Figure 3

Figure 3 shows a unique situation where two separate labeled containers of different types of vaccine are packaged together and given a distinct package number. In this instance, the labeled containers may be injected separately or mixed and injected.

All three of these scenarios (*Figures 1-3*) can be captured using the file-format described in this document.

3.0 File Format:

3.1 Data elements:

In order to capture the information required by 21 CFR 600.81 for direct input into a computer system, a standard file format must be used. The electronic data format adds additional data elements to the current paper reporting format: <u>manufacturer</u>, <u>establishment</u>, <u>product name</u>, <u>National Drug Code (NDC)</u>, <u>starting date</u> and <u>ending date</u>, and <u>package lot</u> number. The starting and ending dates represent the time period of distribution covered by each report. Package lot numbers are provided by the manufacturer who packages separately labeled products, as in *Figure 3*. Except for NDC (which replaces FDA product code), the "additional" data elements are already submitted as additionally requested information. The <u>Strength/Formulation Type</u> is no longer required, since it is implicit in the NDC.

Description	Data-type	Column Width
Manufacturer Name	Character	Min of 1, max of 24
Establishment License No.	Character	4 chars
Product Name	Character	Min of 1, max of 52
National Drug Code (NDC) (optional)	Character	12 characters
Bulk Lot No.	Character	Min of 1, max of 15
Fill Lot No. (optional)	Character	Max of 15
Label Lot No.	Character	Min of 1, max of 15
No. Of Doses	Number	Max of 7 digits (integer ex: 10000)
Distribution Date	Date	"MONTH DD, YYYY"
Expiration Date	Date	"MONTH DD, YYYY"
Package-lot No. (optional)	Character	Max of 15
Starting date	Date	"MONTH DD, YYYY"
Ending date	Date	"MONTH DD, YYYY"

Table 1

3.1.1 Data Element Descriptions

A formal definition of each data-element is provided below:

- <u>Manufacturer Name</u> – The name of the manufacturer (license holder) that produces the product being reported on.
- <u>Establishment License No.</u> – The FDA-assigned establishment license number.
- <u>Product Name</u> – Licensed "FDA generic" product-name ***not the product trade-name***.
- <u>National Drug Code (NDC)</u> – Licensed National Drug Code (NDC) used in product marketing and distribution. Be sure to include the hyphens ('-') in the NDC code.
- <u>Bulk Lot No.</u> - The lot number associated with the largest manufacturing quantity that you track with a lot number.
- <u>Fill Lot No. (optional)</u> – An intermediate size manufacturing unit. Should you have more than 3 lot sizes that you track (more than can be captured with the 3 fields, bulk, fill & label lot), the fill-lot number you provide should be the 2nd-smallest (where label-lot is the smallest size).

- <u>Label Lot No.</u> – The lot number associated with the smallest manufacturing quantity that you track with a lot number. This is the lot number that is on the final container which is distributed in the market for use.
- <u>No. Of Doses</u> – A dose is defined as that amount of biologic product which is usually given at one time. Use this field to report the number of doses as defined.
- <u>Distribution Date</u> - Earliest date product was released to market.
- <u>Expiration Date</u> – Date product expires, and should no longer be in the market for use.
- <u>Package-lot No. (optional)</u> – A small number of manufacturers combine individual products into a "package", and market them together. Those manufacturers should supply the package-lot using this field.
- <u>Starting date</u> – Starting date for information included in the current distribution report (file) being submitted.
- <u>Ending date</u> - Ending date for information included in the current distribution report (file) being submitted.

3.2 Encoding the flat-file

The file your company submits should provide the applicable data in *Table 1*. More specifically, to ensure that your company's data can be processed electronically by the FDA, it is important that the ASCII "flat-file" conform to some rules. First some general rules:

General:

1. The file should be produced as an ASCII DOS file. If you produce the file using a computer not running a Microsoft operating-system (such as Unix, VMS or MVS), please be sure to convert the file to DOS ASCII format prior to submitting it. Different operating-systems use different "end-of-line" characters, and the FDA computers expect files produced as ASCII DOS files.
2. Each "record" or "row" of information should be on a separate line.
3. Use **Table 1** (above) to determine the <u>*order*</u> and <u>*data-type*</u> of columns in each "row" of information you are submitting. For example, the **Manufacturer Name** column is first, and has a data-type of <u>Character</u>, and should be a maximum of 24 characters.
4. All <u>Date</u> columns should be formatted as "MONTH DD, YYYY". (e.g. "January 1, 2000"). Please do not use 2-digit years (such as 99 for 1999)! <u>Date</u>s should be enclosed in double-quotes (unlike <u>Character</u> or <u>Number</u> columns).
5. The <u>Number</u> column (No. Of Doses) should contain only digits, no letters, double-quote (") or comma (,) characters.
6. Columns should be separated by a single comma. For example a <u>Date</u> column followed by a <u>Number</u> column would appear as '"March 3, 2001",10031'. Note that your ASCII file should not include the single-quotes.
7. Character columns can optionally be enclosed in double-quote characters (" - not two single-quotes!). This allows having a comma (,) as part of the product name.
8. There should **not** be a comma at the beginning or end of a "record" or "row" of data.
9. Columns with unknown or non-existent values should appear as only the comma which would normally follow the field.
10. **The use of the convention: NA = "not applicable", NI = "no information" and UNK = "unknown" should be eliminated since <u>Number</u> and <u>Date</u> fields cannot support this.**

In addition to the general rules above, there are some specific rules which apply to the individual fields:

Individual Fields:

1. Manufacturer Name – Character data-type, minimum 1 character, maximum of 24.
2. Establishment License No. - Character data-type, must be 4 characters. Prefix your establishment license number with zeros as required. For example, establishment "3" should be entered as "0003".
3. Product Name - Character data-type, minimum 1 character, maximum of 52.
4. National Drug Code (NDC) (optional) – Character data-type, precisely 12 characters. The NDC will be in one of the following configurations: 4-4-2, 5-3-2, or 5-4-1. In all 3 cases, the NDC is 10 digits, and two hyphens (-), for a total of 12 characters. Be sure to include the dashes (-), thus "0324-0333-01" should not be submitted as "0324033301".
5. Bulk Lot No. - Character data-type, minimum 1 character, maximum of 15.
6. Fill Lot No. (optional) - Character data-type, maximum of 15. If your product involves the use of fill lots, you must include this, otherwise, this field should appear only as a comma (see #9 under *General*, above).
7. Label Lot No. - Character data-type, minimum 1 character, maximum of 15.
8. No. Of Doses – Number data-type, integer from 1 to 7 digits. This number should be proceeded by a minus-sign ('-') if indicating returned doses (example 6 below). Do not include a plus-sign ('+'), and do not include commas (','). As shown in example 2 below, <u>ONLY include the number of doses for the first record</u> when supplying data for a label lot consisting of multiple bulk-lots and fill-lots! Report the complete number of doses in label lot, even if not all of the lot is initially distributed. When reporting the number of doses returned (10% or more) only the establishment, bulk-lot, fill-lot, label-lot and package-lot number along with the number of doses returned is required. **Use a negative number in the <u>No. Of Doses</u> field to indicate returned doses.**
9. Distribution Date – Date, in the format "MONTH DD, YYYY". Note that the double-quotes are required! This date is the first-use distribution date - not the FDA release date.
10. Expiration Date – Date, in the format "MONTH DD, YYYY". Note that the double-quotes are required!
11. Package-lot No. (optional) - Character data-type, maximum of 15. If your product involves the use of package lots, you must include this, otherwise, this field is not used. As shown in example 5, the use of package-lots should have no effect on your reporting of "No. Of Doses". Report the number of doses as normal for each component (lot). If not package lot applies, this field should appear only as a comma (see #9 under *General*, above).
12. Starting date – Date, in the format "MONTH DD, YYYY". Note that the double-quotes are required!
13. Ending date – Date, in the format "MONTH DD, YYYY". Note that the double-quotes are required!

3.3 Examples:

While there are many rules given above, the file produced is actually quite simple after you have produced it once. A number of examples are given below. *Note: For purposes of illustration, **bold typeface** has been used in these examples - do not use in your files (your files <u>must</u> be saved as ASCII text, which does not support fonts, bold typeface, etc.).*

Example 1: Reporting on 3 label-lots. Note that Bulk, fill and label lots are all different. <u>Each</u> label lot indicates the number of doses.

```
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8F99J,89RTY,1000,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,Feel-good,0123-0123-02,01P213,8R45J,89R44,2000,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,Happy-feet,0123-0123-03,01P214,8F22Q,89ASW,10000,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
```

Example 2: A single label-lot from 3 bulk-lots and 3 fill-lots (No. Doses appears only for the first instance of the label-lot)

```
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8F99J,89RTY,1000,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,CureAll,0123-0123-01,01P213,8R45J,89RTY,,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,CureAll,0123-0123-01,01P214,8F22Q,89RTY,,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
```

Example 3: A single label-lot from 3 bulk-lots and 0 fill-lots (No. Doses appears only for the first instance of the label-lot

```
Miracle Cure,1234,CureAll,0123-0123-01,01P875,,89RTY,1000,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,CureAll,0123-0123-01,01P213,,89RTY,,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,CureAll,0123-0123-01,01P214,,89RTY,,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
```

Example 4: A single label-lot from 1 bulk-lots and 3 fill-lots (No. Doses appears only for the first instance of the label-lot)

```
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8F99J,89RTY,1000,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8R45J,89RTY,,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8F22Q,89RTY,,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
```

Example 5: A package lot (two dissimilar label-lots with the same package-lot). Each label lot in the package indicates the number of doses.

```
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8F99J,89RTY,1000,"January 1, 1998","January 1, 2000",P10012,"March 3, 1998","May 3, 1998"
Miracle Cure,1234,Feel-good,0123-0123-02,01P213,8R45J,89R44,2000,"January 1, 1998","January 1, 2000",P10012,"March 3, 1998","May 3, 1998"
```

Example 6: Returned lot of 500 doses (notice the negative No. Doses)

```
Miracle Cure,1234,CureAll,0123-0123-01,01P875,8F99J,89RTY,-500,"January 1, 1998","January 1, 2000",,"March 3, 1998","May 3, 1998"
```

All of the above examples are installed with the FDA-supplied LVU (see below), and placed in the LVU's "home" directory (selected at installation time). The files are named *example1.txt* through *example6.txt*. You are encouraged to use these files as examples for your own submissions.

3.4 Producing the Flat-file:

Even though you can produce the flat-file by hand, or by using a programming language such as SQL, C or FORTRAN, most companies will probably use an off-the-shelf software package to produce their flat-file for submission to the FDA. In fact, the flat-file format documented here was based on the requirements of Oracle's SQL*LOADER and Microsoft's Excel97 packages which are used by in-house staff. Generally, those companies who already use a spreadsheet or database package should find that their package can already produce ASCII "flat-files" which conform to the standards detailed in this document. Readers are urged to exercise caution, however, since many different (and incompatible) ASCII "flat-file" formats are produced by the various 3rd-party products available. It is important to 1) adhere to the rules outlined in this document and 2) run the verification program (described below) at your site prior to submitting your distribution data to the FDA.

4.0 Lot-data Verification Utility (LVU):

In order to make the proper production of your ASCII flat-file as easy as possible you will be provided with a 32-bit Windows95/NT compatible utility program to verify the format of your ASCII file prior to submitting it to FDA. See section "6.0 Support" below for details on obtaining this program.

4.1 Installing the Lot-data Verification Utility (LVU)

In order to run the LVU, you need an IBM Compatible personal computer running Windows95 or Windows NT v4.0 with at least 20 Mb of disk space available. To install the Lot-data Verification Utility (LVU), follow the appropriate steps below. Most users will follow the "LVU obtained from Internet" procedure. In special cases, the LVU will be sent on floppies, in which case you should follow the "LVU on floppy" procedure. In either case, you will need about 20Mb of free space on your PC's hard-disk for the installation.

Important: Before beginning an installation - if you have installed a previous version of the LVU program, you MUST first de-install it before proceeding. To de-install LVU:
- Click on the "Start" button in the lower-left of your Windows95 or NT 4 screen.
- Click on "Settings", then "Control Panel"
- Double-click on "Add/Remove Programs"
- In the list of programs, click on "Lot-data Verification Utility (LVU)", then click on the "Add/Remove" button.
- Follow on-screen instructions
- <u>Important</u>: Remove the directory "C:\Program Files\Lot-data Verification Utility (LVU)". This assumes that you installed LVU to the default LVU drive and directory. If not, remove the directory that you installed LVU to.


LVU obtained from internet:
- If you already have the LVU installed on your PC, click on "Start/Settings/Control Panel" in Windows95. Then select "Add/Remove Programs". Select "Lot-data Verification Utility (LVU)" and click on "OK". Follow on-screen instructions to remove the program, then exit "Add/Remove Programs" and "Control Panel".
- Obtain the LVU program (a file named LVU.EXE) as described in the section **6.0 Support**, below.
- Create an empty "temporary" directory on your PC (or identify an unused directory containing no files).
- Copy the LVU program to the empty "temporary" directory.
- Run the program LVU.EXE in the "temporary" directory. This will create 46 (approximately) files in your "temporary" directory.
- Using "Start/Run" or "Start/Programs/Windows Explorer", run the program "setup.exe" in your temporary directory. Follow on-screen instructions.
- Once the LVU is installed, you no longer need the temporary directory (or the files in it). Delete the files/directory at your discretion.

LVU obtained on floppy:
- If you already have the LVU installed on your PC, click on "Start/Settings/Control Panel" in Windows95. Then select "Add/Remove Programs". Select "Lot-data Verification Utility (LVU)" and click on "OK". Follow on-screen instructions to remove the program, then exit "Add/Remove Programs" and "Control Panel".
- Create a temporary directory, with no other files in it.
- Open a DOS window (Start/Programs/DOS-prompt).
- Using the DOS "cd" command, switch to the temporary directory you created.
- Type "a:lvu" (assuming "a" is your 3.5" floppy drive, substitute your drive letter as appropriate) and follow on-screen instructions. This will create the LVU "setup" files in your temporary file (from a self-extracting ZIP file on the floppies).
- Using "Start/Run" or "Start/Programs/Windows Explorer", run the program "setup.exe" in your temporary directory. Follow on-screen instructions.
- Once the LVU is installed, you no longer need the temporary directory (or the files in it). Delete the files/directory at your discretion.

## *4.2 Running the Verification Program*

The Lot-data Verification Utility (LVU) is designed to be easy to use. Once installed (see above), you will have a selection in your Windows95 "Start/Program" menu listed as "Lot-data Verification Utility (LVU)". Open the LVU by selecting it "Start/Program/Lot-data Verification Utility (LVU)". The LVU selection has a gray icon shaped like a factory. The first screen appears as below:
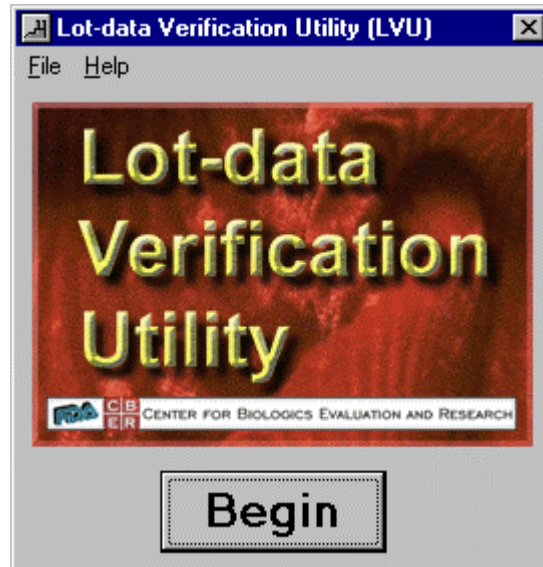
Press the "Begin" button to begin. You will then see the next screen:

Click on the "Browse" button to select the file which contains your distribution data:
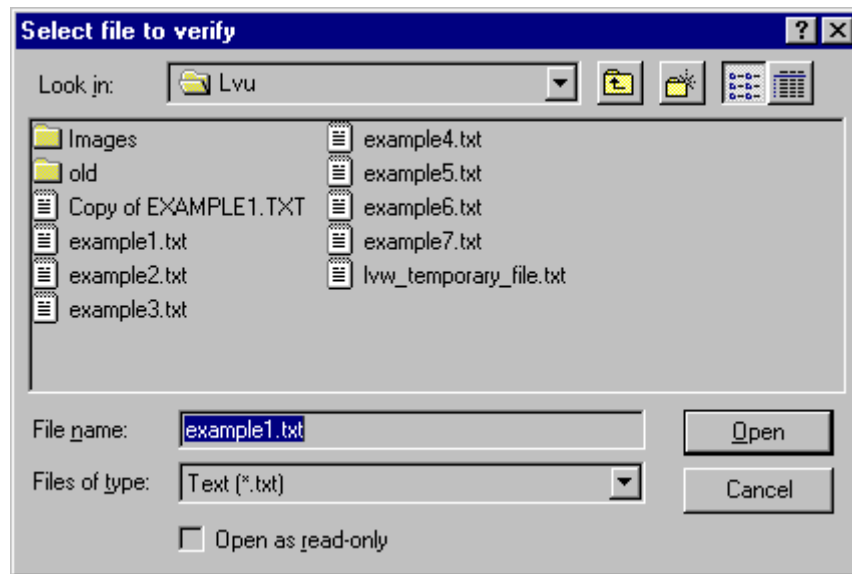
Select your input file, and press "Open" to select a file, or "Cancel" to keep your current selection. In either case, you return to the previous screen:

Click on "Next Step" to proceed (or "Cancel" to stop). You now see a screen as shown below:

You can use the default "Error messages only" which only lists errors in your input file, or click on "All messages" to see all of your input records (lines of ASCII flat-file text), as well as a rather verbose listing of each field from each input record. At first, you may wish to select "All messages" until you have run the LVU once or twice, but you will probably prefer "Error messages only", in general.
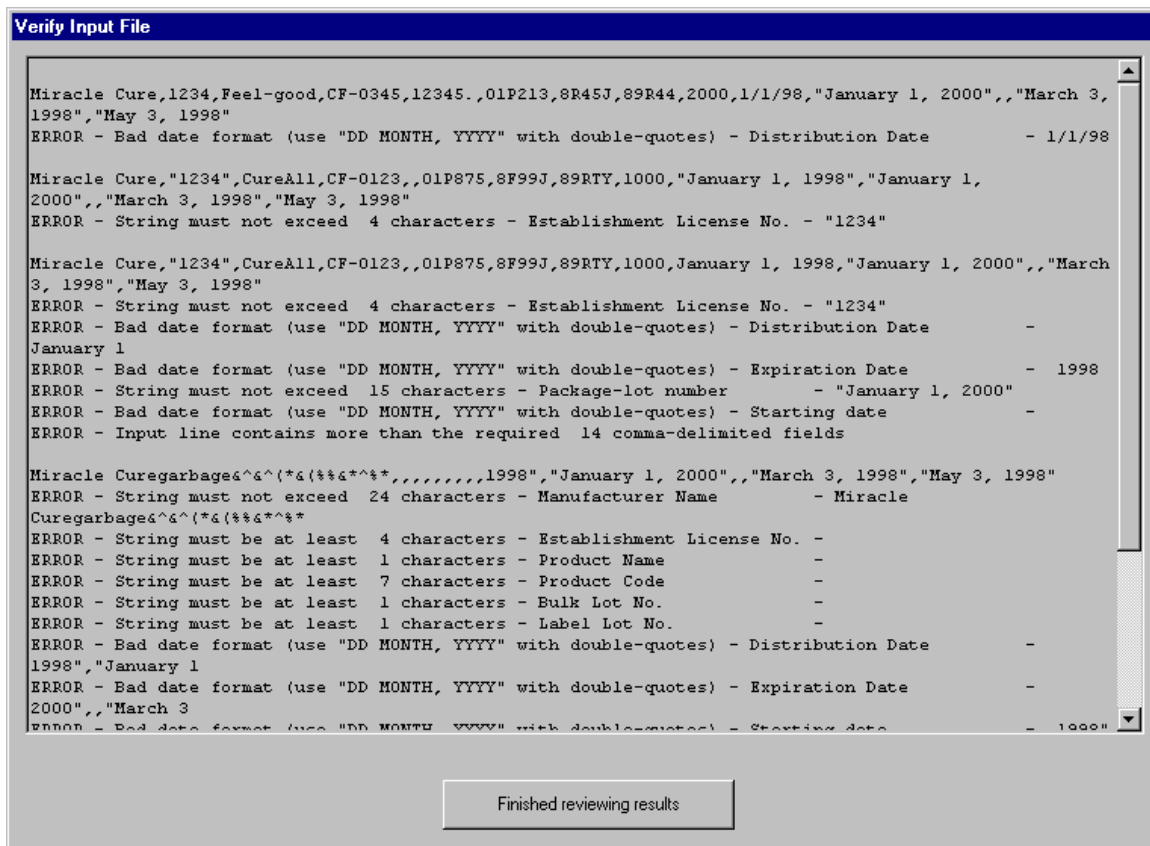
Now, click on "Begin file verification", to get to the next screen:

This is the main screen where you will see the results of your verification check. In this case, the input file had no errors. Here is an example with errors:


In this case, numerous errors are listed. For example, the first record is flagged as an error because 1) the date is provided in the format 1/1/98, rather than "January 1, 1998" and 2) the date is not enclosed in the required double-quotes.

On the screen above, you will notice that the input lines "wrap". Most computer monitors are wide enough that, using your mouse, you can "click and drag" the window so that it is wide enough to display lines without wrapping. You can also "double-click" on the blue "title-bar" (where it says "Verify Input File") to maximize the window (the LVU does this by default).

Click on "Finished reviewing results" to get to the next screen, either:
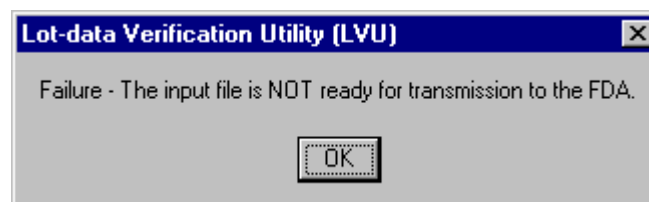
in the case of an error, or:
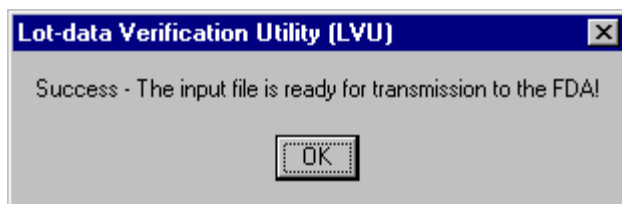
if your file is ready for submission to the Food and Drug Administration (FDA). In either case, you are returned to the main screen:

If your file is ready for submission, select File/Exit to end the program. If your file contains errors, it is generally fastest to open your file in another "window" using your text editor (perhaps notepad) and correct the errors, then click "Begin" on the LVU to check your data again.

5.0 Submission to FDA:

Your completed file should be submitted on 3.5" floppy to:

> Center for Biologics Evaluation and Research (HFM-210)
> Food and Drug Adminstration
> Attn: Biological Products Distribution Reports - Epidemiology Branch
> 1401 Rockville Pike
> Rockville MD 20852-1448

Information concerning lot size constitutes confidential commercial information and will not be publicly disclosed in response to a request under the Freedom of Information Act without the consent of the manufacturer.

6.0 Support:

A web-page is being provided as a means for distributing the verification program, as well as to provide additional assistance to manufacturers in submitting their distribution data to the FDA. Please visit the URL (web-page) at:

http://www.fda.gov/cber/vaers/lvu.htm

for additional information.

The FDA is eager to complete the transition to electronic submission of lot-distribution. In the event the web-page does not provide sufficient assistance, or you do not have access to the Internet, please use the following contact for support, and/or to obtain the verification program:

Phil Perucci, Software Developer   - 301-827-6062

Comments on the usability of this process and suggestions for improvement are welcome.

7.0 Change History

Changes to the original flat-file format and LVU program (first release was version 1.0.2) are as follows:

Version 1.0.3:

- Character columns can now be enclosed in double-quote (") characters. This allows having a comma (,) as part of a product name.

- Corrected error message when wrong date format is used.

- Lots distributed and lots returned can now be included in the same electronic file.

- Product-code eliminated, and replaced with NDC

- Strength/formulation eliminated (implicit in NDC)

Version 1.0.4:

- Fixed bug which caused "number of doses" larger than 32767 to fail

- Now checks format of NDC code

- Allows printing of results